

### Amendments to the Claims

The current status of all claims is listed below and supercedes all previous lists of claims.

Please cancel claims 1-104 without prejudice to the applicants' right to reinstate those claims or pursue the subject matter of the cancelled claims in a further application.

1-104. (Cancelled)

Please add claims 105-176 as follows.

105 (New). A method of inhibiting mycobacterial growth in a patient comprising administering an amount of a composition comprising an inhibitor of Rel<sub>Mtb</sub>.

106 (New). The method of claim 105 wherein said inhibitor inhibits the hydrolytic or synthetic activity of Rel<sub>Mtb</sub>.

107 (New). The method of claim 105 wherein said mycobacteria is *M. tuberculosis*.

108 (New). The method of claim 105 wherein said inhibitor of Rel<sub>Mtb</sub> is coadministered with at least one antibiotic.

109 (New). The method of claim 108 wherein said at least one additional antibiotic is isoniazid, rifampin, streptomycin, pyrazinamide or ethambutol.

110 (New). The method of claim 105 wherein said amount is an effective amount to ameliorate a mycobacterial infection in said patient.

111 (New). The method of claim 105 wherein the inhibitor is an antisense oligonucleotide at least 90% homologous to the complement of a nucleic acid molecule encoding a *M. tuberculosis* Rel<sub>Mtb</sub> polypeptide (SEQ ID NO:7, 8, 9, 10, 11, 12, or 13), wherein said antisense oligonucleotide specifically hybridizes to the nucleic acid molecule and inhibits *M. tuberculosis* Rel<sub>Mtb</sub> mRNA levels by at least 50% in *M. tuberculosis*.

112 (New). A recombinant vaccine comprising a nucleotide sequence that encodes *M. tuberculosis* immunogen operably linked to regulatory elements, wherein said immunogen comprises Rel<sub>Mtb</sub> or a fragment thereof.

113 (New). The recombinant vaccine of claim 112 wherein said immunogen comprises SEQ ID NOs, 14, 15, 16, 17, 18, 19, or 20, or a fragment thereof.

114 (New). A method of inducing an immune response in a patient against a pathogen comprising administering to said patient a recombinant vaccine of claim 112.

- 115 (New). A method of inducing an immune response in an animal comprising administering an immunogenic composition comprising an attenuated *M. tuberculosis*.
- 116 (New). The method of claim 115 wherein said attenuated *M. tuberculosis* comprises an inactivated Rel<sub>Mtb</sub> gene.
- 117 (New). The method of claim 115 wherein said attenuated mycobacteria tuberculosis comprises a mutated Rel<sub>Mtb</sub> protein, wherein said mutated Rel<sub>Mtb</sub> protein comprises a sequence of SEQ ID NO: 8, 9, 10, 11, 12, or 13, or a fragment thereof.
- 118 (New). The method of claim 117 wherein the mutated Rel<sub>Mtb</sub> protein has a synthetic activity reduced by at least 50% compared to non-mutated Rel<sub>Mtb</sub> protein.
- 119 (New). The method of claim 117 wherein the mutated Rel<sub>Mtb</sub> protein has a hydrolytic activity reduced by at least 50% compared to non-mutated Rel<sub>Mtb</sub> protein.
- 120 (New). The method of claim 117 wherein said mutated Rel<sub>Mtb</sub> protein has diminished hydrolytic and synthetic activity compared to non-mutated Rel<sub>Mtb</sub> protein..
- 121 (New). The method of claim 117 wherein said mutated Rel<sub>Mtb</sub> protein has activated hydrolytic or activated synthetic activity, or activated hydrolytic and activated synthetic activity, compared to non-mutated Rel<sub>Mtb</sub> protein.
- 122 (New). The method of claim 115 wherein said animal is a mouse, monkey, or human.
- 123 (New). A method of inducing an immune response in a patient comprising administering to said patient an immunogenic composition comprising a polypeptide, said polypeptide comprising a Rel<sub>Mtb</sub> protein or fragment thereof.
- 124 (New). The method of claim 123 wherein said polypeptide comprises one or more sequences of SEQ ID NOs: 7, 8, 9, 10, 11, 12, or 13, or fragments thereof.
- 125 (New). The method of claim 123 wherein said polypeptide has diminished synthesis activity.
- 126 (New). The method of claim 123 wherein said polypeptide has diminished hydrolysis activity.
- 127 (New). The method of claim 123 wherein said polypeptide has synthetic activity.
- 128 (New). The method of claim 123 wherein said polypeptide has hydrolytic activity.
129. The method of claim 123 wherein said polypeptide has hydrolytic and synthesis activity.
- 130 (New). The method of claim 123 wherein said polypeptide has diminished hydrolytic and synthetic activity.

- 131 (New). A method of modulating transcription in *M. tuberculosis* comprising administering to said *M. tuberculosis* a composition comprising a modulator of Rel<sub>Mtb</sub>.
- 132 (New). The method of claim 131 wherein said modulator is an antibody, peptide, polypeptide, small molecular weight compound, antisense compound, or RNAi compound.
- 133 (New). The method of claim 131 wherein said modulator inhibits the synthetic or hydrolytic activity of Rel<sub>Mtb</sub>.
- 134 (New). The method of claim 131 wherein said modulator inhibits the hydrolytic and the synthetic activity of Rel<sub>Mtb</sub>.
- 135 (New). The method of claim 131 wherein said modulator activates hydrolytic activity, synthetic activity, or both, of the Rel<sub>Mtb</sub> protein.
- 136 (New). An isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising a fragment of a Rel<sub>Mtb</sub> protein, said fragment having hydrolytic or synthetic activity.
- 137 (New). The isolated polynucleotide of claim 136 wherein said fragment has synthetic and hydrolytic activity.
- 138 (New). The isolated polynucleotide of claim 136 wherein said hydrolytic and/or synthetic activity is not increased or decreased by the Rel<sub>Mtb</sub> activating complex (RAC).
- 139 (New). The isolated polynucleotide of claim 136 wherein said fragment has diminished synthetic activity, hydrolytic activity, or synthetic and hydrolytic activity.
- 140 (New). The isolated polynucleotide of claim 136 wherein said nucleotide sequence comprises SEQ ID NOs: 15, 16, 17, 18, 19, or 20.
- 141 (New). The isolated polynucleotide of claim 136 wherein said polypeptide comprises SEQ ID NOs 9, 10, 11, 12, 13, or 14.
- 142 (New). An expression vector comprising a nucleic acid molecule of claim 136.
- 143 (New). The expression vector of claim 142 wherein said vector is a plasmid or a viral particle.
- 144 (New). The expression vector of claim 142 wherein said vector is selected from the group consisting of adenoviruses, baculoviruses, parvoviruses, herpesviruses, poxviruses, adeno-associated viruses, Semliki Forest viruses, vaccinia viruses, and retroviruses.
- 145 (New). The expression vector of claim 142 wherein said nucleic acid molecule is operably connected to a promoter selected from the group consisting of simian virus 40, mouse mammary tumor virus, long terminal repeat of human immunodeficiency virus, maloney virus, cytomegalovirus immediate early promoter, Epstein Barr virus, rous sarcoma

virus, human actin, human myosin, human hemoglobin, human muscle creatine kinase, and human metallothionein.

146 (New). A host cell transformed with an expression vector of claim 142.

147 (New). The transformed host cell of claim 146 wherein said cell is a mycobacterial cell, a bacterial cell, yeast, an insect cell or a mammalian cell.

148 (New). The transformed host cell of claim 147 wherein said cell is *M. tuberculosis*, *M. smegmatis*, *E. coli*, *S. cerevisiae*, or *S. frugiperda*.

149 (New). The transformed host cell of claim 147 wherein mammalian cell is selected from the group consisting of chinese hamster ovary cells, HeLa cells, African green monkey kidney cells, human HEK-293 cells, and murine 3T3 fibroblasts.

150 (New). An antisense oligonucleotide at least 90% homologous to the complement of a nucleic acid molecule encoding a *M. tuberculosis* Rel<sub>Mtb</sub> polypeptide (SEQ ID NO:7, 8, 9, 10, 11, 12, or 13), wherein said antisense oligonucleotide specifically hybridizes to the nucleic acid molecule and inhibits *M. tuberculosis* Rel<sub>Mtb</sub> mRNA levels by at least 75% in *M. tuberculosis*.

151 (New). The antisense oligonucleotide of claim 150, wherein said antisense oligonucleotide hybridizes within the 5'-UTR, 3'-UTR, or coding region of SEQ ID NO:7.

152 (New). The antisense oligonucleotide of claim 150, wherein said antisense oligonucleotide is from about 10 to about 30 nucleobases in length.

153 (New). A composition comprising a nucleic acid molecule of claim 150 and a pharmaceutically acceptable carrier or diluent.

154 (New). A composition comprising an expression vector of claim 142 and a pharmaceutically acceptable carrier or diluent.

155 (New). A method of producing a polypeptide that comprises a fragment of SEQ ID NO:7, said method comprising:

- a) introducing an expression vector of claim 142 into a compatible host cell;
- b) growing said host cell under conditions for expression of said polypeptide; and
- c) recovering said polypeptide.

156 (New). The method of claim 155 wherein said host cell is lysed and said polypeptide is recovered from the lysate of said host cell.

157 (New). An isolated polypeptide fragment of Rel<sub>Mtb</sub> encoded by a nucleic acid molecule comprising an amino acid sequence with selected from the group consisting of SEQ ID NOs 14, 15, 16, 17, 18, and 19.

158 (New). The polypeptide of claim 157 wherein said polypeptide comprises a sequence at least 90% homologous to SEQ ID NO: 8, 9, 10, 11, 12, or 13.

159 (New). The polypeptide of claim 157 wherein said polypeptide comprises an amino acid sequence of SEQ ID NO: 8, 9, 10, 11, 12, or 13.

160 (New). An isolated polypeptide fragment of Rel<sub>Mtb</sub>, wherein said fragment has hydrolytic and/or synthetic activity, said hydrolytic and/or synthetic activity is not increased or decreased by more than 10% by the Rel<sub>Mtb</sub> activating complex (RAC).

161 (New). The isolated polypeptide fragment of claim 160 wherein said fragment comprises an amino acid sequence of SEQ ID NO: 8, 9, 10, 11, 12, or 13.

162 (New). A composition comprising a polypeptide of claim 160 and an acceptable carrier or diluent.

163 (New). An isolated antibody which binds to an epitope on a polypeptide of claim 160.

164 (New). The antibody of claim 163 wherein said antibody is a monoclonal antibody.

165 (New). A composition comprising an antibody of claim 163 and an acceptable carrier or diluent.

166 (New). A method of identifying modulators of Rel<sub>Mtb</sub> activity comprising:

- a) contacting Rel<sub>Mtb</sub> with a potential modulator; and
- b) measuring the activity of Rel<sub>Mtb</sub>

wherein if an activity of Rel<sub>Mtb</sub> is inhibited then the modulator is an inhibitor of Rel<sub>Mtb</sub> activity, and if an activity of Rel<sub>Mtb</sub> is increased the modulator is an activator of Rel<sub>Mtb</sub> activity.

167 (New). A method of protecting a patient from a *M. tuberculosis* infection comprising administering to said patient an amount of a composition comprising a Rel<sub>Mtb</sub> modulator effective to protect the animal from *M. tuberculosis* infection.

168 (New). A method of modulating growth of a pathogen comprising administering to said pathogen an amount of a composition comprising a Rel<sub>Mtb</sub> modulator effective to inhibit growth of said pathogen.

169 (New). The method of claim 168 wherein said amount of a composition comprising a modulator effective to protect the animal from *M. tuberculosis* infection inhibits the growth of *M. tuberculosis* by at least 50% in an *in vitro* assay.

170 (New). The method of 169 wherein said *in vitro* assay measures oxygen consumption, or carbon consumption.

171 (New). A method of inhibiting dormancy in *M. tuberculosis* comprising contacting said *M. tuberculosis* with a composition comprising a modulator of Rel<sub>Mtb</sub>, said modulator selected from the group consisting of an antibody, peptide, polypeptide, small molecular weight compound, antisense compound, or RNAi compound.

172 (New). The method of claim 171 wherein said modulator inhibits the synthetic or hydrolytic activity of Rel<sub>Mtb</sub>.

173 (New). The method of claim 171 wherein said modulator inhibits the hydrolytic and synthetic activity of Rel<sub>Mtb</sub>.

174 (New). The method of claim 171 wherein said modulator activates hydrolytic activity, synthetic activity, or both of the Rel<sub>Mtb</sub> protein.

175 (New). An attenuated *M. tuberculosis* comprising an inactivated Rel<sub>Mtb</sub> gene, wherein said inactivated Rel<sub>Mtb</sub> gene encodes for a Rel<sub>Mtb</sub> protein with diminished synthetic activity, hydrolytic activity, or both, said polypeptide having an amino acid sequence at least 90% homologous to SEQ ID NOs 8, 9, 10, 11, 12, or 13.

176 (New). The attenuated *M. tuberculosis* of claim 175 wherein said inactivated Rel<sub>Mtb</sub> gene has a nucleotide sequence of SEQ ID NOs 14, 15, 16, 17, 18, or 19.